REMARKS

Claims 1-29 are pending in the application. Claims 2 and 6-29 are withdrawn by the Examiner as directed to a non-elected invention. Claims 1 and 3-5 are currently under examination. Claims 1-10, 12, 16, 20-21, and 25-28 have been amended. Reconsideration of the claims in view of these amendments and remarks is respectfully requested.

I. Unity of Invention

The Examiner maintained and made final restriction of the claims first presented in the Restriction Requirement mailed June 27, 2008. Applicants continue to traverse the restriction and have concurrently submitted a Petition to the Director requesting withdrawal of the Restriction Requirement and consideration of the claims under the appropriate Unity of Invention standard, as stated in PCT Rule 13 and explained in the PCT International Search and Examination Guidelines, Chapter 10, prepared March 24, 2004.

Applicants respectfully assert the Examiner has failed to apply the required Unity of Invention standard in applying a U.S. Restriction of sequences in a manner that permits examination of only one sequence. While "each sequence is a patentably distinct invention", where the inventions are related and share one or more common technical feature that contributes to the prior art, Rule 13.2 permits examination of the inventions as a whole.

1. PCT Rule 13 should be applied

Applicants assert Unity of Invention according to PCT Rules 13.1 and 13.2 should properly be applied to this application, as the application was submitted under 35 U.S.C.§ 371as the U.S. national stage of PCT/DK/04/00478.

2. PCT Rule 13 - Inventions sharing a common special technical feature

Rule 13.2 specifies that unity of invention applies where there is a technical relationship between the claimed inventions involving one or more of the same or corresponding special technical features.

The phrase "special technical features" is defined as "those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art" (PCT Rule 13.2).

The determination that a particular technical feature makes a contribution over the prior art is made with respect to novelty and inventive step (ISPE para. 10.02).

3. The inventions are technically related by one or more technical feature

The inventions described and claimed are related by structural and functional features. Common technical features include:

a. common structural features:
   i. an amount of sequence identity (at least 70%);
   ii. structural domains (Signal peptide, ECD, kinase domain);
   iii. structural features (2 or 3 LysM motifs in ECD);

b. common functional features:
   i. members of a Nod-factor binding element;
   ii. specific Nod-factor binding properties for perception of strain-specific Nod factors;
   iii. trigger signaling pathway for nodulation;
   iv. lead to activation of nodulin gene expression;
   v. confer selective rhizobial strain recognition;
   vi. confer nodulation to non-nodulating plants

c. common structural feature is required for common functional activity
   i. selective rhizobial strain recognition requires LysM motifs.

4. Technical features contribute over the prior art

a. The Examiner indicated in the Office Action dated November 21, 2008 that claim 3 (reciting SEQ ID NOs: 8, 15, 32, 40, and 48) and claim 5 (reciting SEQ ID NOs: 24, 25, 52, 54, and 8, 15, 32, 40 and 48) are free of the prior art.

b. The pending art rejections relate to polypeptide fragments. The claims as amended limit the recited fragments to those containing at least two LysM motifs and retain selective binding to Nod-factor.
c. The Nod-factor binding proteins having the ability to discriminate between and selectively bind chemically modified Nod factors are new.
d. Prior art fails to disclose specific binding proteins with sequence, LysM motifs, and strain-specific perception and binding of Nod-factors.

Applicants direct the Examiner to the Examples contained in the PCT International Search and Examination Guidelines, Chapter 10, for example, those discussing claims to multiple distinct but related sequences such as Examples 32 and 33. Each of these examples frames a specific approach to determining unity of invention:

> The sequences "would be regarded as having the same or corresponding technical feature if the alternatives have a common property or activity and shared a significant structural element that is essential to the common property". (PCT ISEG, Chapter 10, 10.52, 53).

Accordingly, Applicants submit inventions recited in the instant claims share at least one common property (for example, selective binding of Nod-factors for strain-specific perception of Nod-factors and initiation of nodulation in plants), and at least one shared significant structural element that is required for the common property (for example, sequence identity and extracellular LysM motifs). As these features are not in the prior art, Applicants submit the instant inventions (first and second Nod-factor binding proteins) would be regarded as having the same or corresponding technical feature, and therefore satisfy the PCT Rule 13 criteria for Unity of Invention. Withdrawal of the Restriction/Unity requirement examination of the claims as a whole (claims 1- 24) is respectfully requested.

II. Amendments to Specification

The specification has been amended to remover hyperlinks and add SEQ ID NOs. as requested.

III. Priority

Applicants note the Examiner has accorded the priority date of July 3, 2003. The status of the provisional application has been amended.

IV. Claim Objections

Claims 1 and 3-5 are objected to because they recite non-elected sequences or are dependent on non-elected sequences. Applicants request the claims as amended, remain intact with the listed sequences while the Petition for Unity is considered.

V. Definiteness – 35 USC § 112, second paragraph

Claims 1 and 3-5 are rejected under 35 U.S.C. 112, second paragraph, as indefinite. In particular, the Examiner has objected to the following claim terms: "(NFR1)", "specific", "identical", "functional fragement", and to claim 4 and 5(b). The claims have been amended to remove the terms, correct claim 5, and clarify that claim 4 limits claim 1. Removal of these objections is requested.

VI. Enablement – 35 USC § 112, first paragraph,

The Examiner has rejected claims 1 and 4 under 35 U.S.C. 112, first paragraph, suggesting that, while being enabling for SEQ ID NO:8, the specification does not enable a scope of 60% identity to SEQ ID NO:8 and fragment thereof. In particular, the examiner objects to the term "specific" Nod-factor binding activity, and suggests the Applicants have not provided working examples or guidance regarding tolerance of mutations. Applicants respectfully traverse this rejection.

Nod-factor binding properties are defined on page 16 of the specification:

> **Nod-factor binding properties**: are characteristic of NFR1 and NFR5 polypeptides and are particularly associated with the extracellular domain of said NFR polypeptides, which comprise LysM domains. The binding of Nod factors by the extracellular domain of NFR polypeptides is specific, such [that] the NFR polypeptides can distinguish between the strain-specific chemically modified forms of Nod-factor. (p16, lines7-12).

Beginning on page 26 and extending to page 54, the specification includes 5 working examples detailing the cloning and sequencing of two families of Nod-factor binding polypeptides (NFR5 and NFR1). Each polypeptide was first isolated from *Lotus japonicus*, cloned and sequenced, and mutations mapped to the sequence. (see Figures 1-12 and data Tables 1-13. Additional family members were obtained PCR amplification and sequencing, isolating a variety of NFR5 and NFR1 genomic clones and mutants from lotus, pea, black bean, soybean, among others.

Primary sequence and structural domains were determined and are shown, for example, in Figures 1, 2, 3, 5, 6, 11, and 12. Functional studies in plants demonstrating wild type and mutant Nod-factor binding polypeptide activity in a variety of species were performed and reported. These studies included *in planta* replacement of Nod-factor binding protein in mutants by inserting transgenes, for example into non-nodulating plants transforming them into plants capable of nodulation, as well as using transgenes to alter the Nod-factor/rhizobial selectivity (See Examples 4 and 5).

NFR1 and NFR5 family members share common structural features and common structural alignment, including a similar domain structure comprising an N-terminal signal peptide, an extracellular domain having 2 or 3 LysM-type motifs, a transmembrane domain, an intracellular domain comprising a kinase domain characteristic of serine/threonine kinases. The extracellular domain of NFR proteins is the primary determinant of specificity of Nod-factor recognition (see, for example, page 15 lines 3-14).

NFR5 protein sequence alignments show 70-86% primary amino acid sequence identity, while nucleic acid sequence identity is about 80-90% (e.g. Lotus, Glycine and

Phaseolus, Tables 1, 2 page 18). NFR1 alignments similarly show 73-79% amino acid identity, with 83-87% nucleic acid sequence identity. The conserved sequences of the LysM motifs are shown in Figures 2 and 6.

Methods for isolating genes and cDNAs encoding NFR1 and NFR5, particular comparisons of sequences and homology, expression in transgenic plants, are all described, beginning at page 21, with particular examples.

Applicants submit the working examples and specification provide adequate guidance to one of skill in the art, fully enabling the making and using of the claimed invention over its full scope, including working examples demonstrating by transgene hybrid gene providing wild type, functional NFR5 and/or NFR1 to mutant, non-nodulating plants as well that strain specificity of the Nod-factor binding element (selective Nod-factor perception) is determined by the extracellular domain of the component NFR polypeptides.

Removal of the rejection based on enablement is requested.

VII. Written Description – 35 USC § 112, first paragraph

Claims 1 and 4 and also are rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement. In particular, the Examiner asserts a representative number of species has not been disclosed, and that it is unpredictable what other sequence structures within the 60% identity would also have specific Nod-factor binding activity. Applicants respectfully traverse this rejection.

Written description requires that the invention be so described as to inform a person of skill in the art that the inventor was in possession of the invention. As discussed above for enablement, Applicants have provided numerous representative NFR5 and NFR1 polypeptides, together with description of functional and non-functional mutant forms, a teaching that selective binding by these Nod-factor binding proteins to chemically modified Nod-Factor is conferred by the LysM motifs in the ECD, as well as guidance provided to obtain and sequence multiple forms of the polypeptides.

Accordingly, Applicants submit the depth of the disclosure, the variety and scope of the NFR5 and NFR1 Nod-factor binding polypeptides described in the specification is more than adequate to inform the skilled artesian that the inventor was in full possession of the invention, including molecules having at least 70% identity to SEQ ID NO:8.

VIII. Prior Art Rejections – 35 USC § 102

Claims 1 and 4 are rejected under 35 U.S.C. §102(b) as being anticipated by Stracke et al. (Nature, Vol. 417, June 27, 2002, pp. 959-962) or Niebel et al. (MPMI, Vol. 10, No. 1, Jan 1997, pp. 132-134). Etzler, US 6465716 is also cited as anticipating the claims. In particular, the Examiner notes the fragment size and specific nod-factor binding property are not defined by the specification, and "Thus the claims read on any Nod-factor binding protein". Applicants respectfully traverse the rejection as it may be applied to the amended claims.

Nieble discloses a chemical approach to finding the Nod-factor binding polypeptide, using microsomal fractions and radiolabeled Nod-factor. No genes or proteins are identified or isolated from the fractions.

Stracke discloses SYMRK, a protein required for an early step in the common symbiotic signaling pathway, and located downstream of perception and binding of microbial signal molecules (see page 4; see also Markmann 2008 PLOS Biology 6:e68, at page 0500).

Etzel discloses NBP46, a Nod-factor binding lectin reported to confer the ability to bind carbohydrates in the rhizobial cell wall, conferring apyrase activity.

Applicants also note the Examiner has indicated in the outstanding Office Action that claims 3 and 5 are free of the prior art.

The claims have been amended to clarify what is disclosed in the specification, namely that rhizobial selective binding of the Nod-factor binding polypeptides to Nod-factor, e.g., nod factor perception by the Nod-factor binding polypeptides, is requires the LysM motifs of the extracellular domain (See Example 5, section 4).

As none of the cited references teach of suggest the claimed invention, and in view of the amendments to the claims, Applicants submit the claims are free of the prior art. Removal of this rejection is requested.

IX. Conclusion

In light of the forgoing amendments and remarks, Applicants respectfully request recognition of the unity of the claims, reconsideration of the claims under a unity of invention standard, and allowance of the claimed subject matter. A prompt notice to these effects is respectfully solicited.

If there are any remaining questions, or if clarification of any of the amendments and remarks is needed, the Examiner is invited to contact the undersigned at the number listed below.

Respectfully submitted,

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